

Claims

1. A method for distinguishing AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q in a sample, the method comprising determining the expression level of markers selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2,

wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.1 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.1 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.2 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.2 having a positive fc value,

is indicative for the presence of AML₊13 when AML₊13 is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.3 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.3 having a positive fc value,

is indicative for the presence of AML₊8 when AML₊8 is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.4 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.4 having a positive fc value,

is indicative for the presence of AML_-7 when AML_-7 is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.5 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.5 having a positive fc value,

is indicative for the presence of AML_5q when AML_5q is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.6 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.6 having a positive fc value,

is indicative for the presence of AML_9q when AML_9q is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.7 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 1.7 having a positive fc value,

is indicative for the presence of AML_normal when AML_normal is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.1 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.1 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from AML₊13,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.2 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.2 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from AML₊8,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.3 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.3 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from AML₋7,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.4 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.4 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from AML_{5q},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.5 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.5 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from AML_{9q},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.6 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.6 having a positive fc value,

is indicative for the presence of AML₊11 when AML₊11 is distinguished from AML_{normal},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.7 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.7 having a positive fc value,

is indicative for the presence of AML₊13 when AML₊13 is distinguished from AML₊8,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.8 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.8 having a positive fc value,

is indicative for the presence of AML₊13 when AML₊13 is distinguished from AML₋7,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.9 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.9 having a positive fc value,

is indicative for the presence of AML₊13 when AML₊13 is distinguished from AML_{5q},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.10 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.10 having a positive fc value,

is indicative for the presence of AML_+13 when AML_+13 is distinguished from AML_9q,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.11 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.11 having a positive fc value,

is indicative for the presence of AML_+13 when AML_+13 is distinguished from AML_normal,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.12 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.12 having a positive fc value,

is indicative for the presence of AML_+8 when AML_+8 is distinguished from AML_-7,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.13 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.13 having a positive fc value,

is indicative for the presence of AML_+8 when AML_+8 is distinguished from AML_5q,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.14 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.14 having a positive fc value,

is indicative for the presence of AML₊8 when AML₊8 is distinguished from AML_{9q},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.15 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.15 having a positive fc value,

is indicative for the presence of AML₊8 when AML₊8 is distinguished from AML_{normal},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.16 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.16 having a positive fc value,

is indicative for the presence of AML₋7 when AML₋7 is distinguished from AML_{5q},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.17 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.17 having a positive fc value,

is indicative for the presence of AML₋7 when AML₋7 is distinguished from AML_{9q},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.18 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.18 having a positive fc value,

is indicative for the presence of AML₋7 when AML₋7 is distinguished from AML_{normal},

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.19 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.19 having a positive fc value,

is indicative for the presence of AML_5q when AML_5q is distinguished from AML_9q,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.20 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.20 having a positive fc value,

is indicative for the presence of AML_5q when AML_5q is distinguished from AML_normal,

and/or wherein

a lower expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.21 having a negative fc value, and/or

a higher expression of at least one polynucleotide defined by at least one of the numbers 1 to 50 of Table 2.21 having a positive fc value,

is indicative for the presence of AML_9q when AML_9q is distinguished from AML_normal.

2. The method according to claim 1 wherein the polynucleotide is labelled.
3. The method according to claim 1, wherein the label is a luminescent, preferably a fluorescent label, an enzymatic or a radioactive label.
4. The method according to claim 1, wherein the expression level of at least two, preferably of at least ten, more preferably of at least 25, most preferably of 50 of the markers of at least one of the Tables 1.1-2.21 is determined.

5. The method according to claim 1, wherein the expression level of markers expressed lower in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold lower, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold lower in the first subtype.

6. The method according to claim 1, wherein the expression level of markers expressed higher in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold higher, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold higher in the first subtype.

7. The method according to claim 1, wherein the sample is from an individual having AML.

8. The method according to claim 1, wherein at least one polynucleotide is in the form of a transcribed polynucleotide, or a portion thereof.

9. The method according to claim 8, wherein the transcribed polynucleotide is a mRNA or a cDNA.

10. The method according to claim 8, wherein the determining of the expression level comprises hybridizing the transcribed polynucleotide to a complementary polynucleotide, or a portion thereof, under stringent hybridization conditions.

11. The method according to claim 1, wherein at least one polynucleotide is in the form of a polypeptide, or a portion thereof.

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12. The method according to claim 8, wherein the determining of the expression level comprises contacting the polynucleotide or the polypeptide with a compound specifically binding to the polynucleotide or the polypeptide.
13. The method according to claim 12, wherein the compound is an antibody, or a fragment thereof.
14. The method according to claim 1, wherein the method is carried out on an array.
15. The method according to claim 1, wherein the method is carried out in a robotics system.
16. The method according to claim 1, wherein the method is carried out using microfluidics.
17. Use of at least one marker as defined in claim 1, for the manufacturing of a diagnostic for distinguishing AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q.
18. The use according to claim 17 for distinguishing AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q in an individual having AML.
19. A diagnostic kit containing at least one marker as defined in claim 1, for distinguishing AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q, in combination with suitable auxiliaries.

20. The diagnostic kit according to claim 19, wherein the kit contains at least one reference for the AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q.

21. The diagnostic kit according to claim 20, wherein the reference is a sample or a data bank.

22. An apparatus for distinguishing AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q in a sample containing a reference data bank.

23. The apparatus according to claim 22, wherein the reference data bank is obtainable by comprising

- (a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2, and
- (b) classifying the gene expression profile by means of a machine learning algorithm.

24. The apparatus according to claim 23, wherein the machine learning algorithm is selected from the group consisting of Weighted Voting, K-Nearest Neighbors, Decision Tree Induction, Support Vector Machines, and Feed-Forward Neural Networks, preferably Support Vector Machines.

25. The apparatus according to claim 22, wherein the apparatus contains a control panel and/or a monitor.

26. A reference data bank for distinguishing AML subtypes with different gene dosages selected from AML-TRI8, AML-TRI11, AML-TRI13, AML-MO7, and/or AML-DEL5q obtainable by comprising

(a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2, and

(b) classifying the gene expression profile by means of a machine learning algorithm.

27. The reference data bank according to claim 26, wherein the reference data bank is backed up and/or contained in a computational memory chip.